January 10, 1949.

Dr. J. Monod,
Institut Pasteur,
Paris.

Dear Jacques.

I have been waiting to see your manuscript before replying, but evidently it has been delayed.

I did some work on drug resistance in K-12 a couple of years ago, and as I recall did manage to select for recombinants using azide and streptomycin, but this work was not pushed very far, and I do not have those stocks. Using nutritional selection, it was easy to show that these resistance factors segregated and also recombined in prototrophs. I was unable then to get any very cleacut proflavine resistant mutants. If you would see any advantage in the attempt , I would be glad to try to see whether I could succeed in crossing the strains with which you are having difficulty.

There is very little more I can add to gene enzyme studies that I have not already written. I believe that I have already told you of my kinetic studies of the Na effect on K-12 lactase. We are in process of extracting the enzyme, like yourself, from a variety of mutants.

One point worth mentioning, au passant, is that one mutant class (Lac_1^-) which has hitherto appeared to be rigidly lactose-negative, is capable of adapting to produce a galactosidase which will attack lactase, but only in the presence of butyl galactoside, not with lactose. This is a further

indication that the genetic effects are mostly on the adaptation mechanisms, and, for the most part, do not have to do directly with the specificities of the enzymes. A further indication of this is given by the temperature mutant referred to in the enclosed abstract. In this mutant, the effect of temperature is not on the activity of the enzyme but on its formation.

Before we were aware of your findings on amylomaltase, Doudoroff and I had been working on the mechanism of maltose utilization in the suppressor combination Lac_3-S_m/ which is Mal-Glu/. Your findings have been confirmed, and maltose is assimilated via polysaccharide both in the suppressor stock and in K-12. However, we cannot account for the total utilization of maltose by intact cells of the suppressor. Glucose accumulates in substantially equimolar proportions when maltose is fermented by dry cell preps. containing amylomaltase, but does not with intact cells, although glucose supplied to these cells is not touched. Our paper has been submitted to the Jour, Biol. Chem., but probably will not be in print for some time.

Until recently, I had been extracting lactase in Green's wet crushing mill, but at Doudoroff's suggestion I have now merely been drying the cells at room temperature over P_2O_5. Lactase is very readily extracted with dilute buffer from the dried cells. This method has the great advantage of great flexibility, and is very efficient.

We were doing some experiments lately on getting antibodies to lactase, but with no encouragement so far.

With best regards,

Cordially,

Joshua Lederberg

~ Interzygote